PH impact Lyme disease: approach in the Netherlands

Cees van den Wijngaard
Agnetha Hofhuis, Florianne Bauer, Wilfrid van Pelt
Content

1. Lyme in the Netherlands
2. Doctors and patient questionnaires
3. Web-based prospective surveillance
4. Clinical study
Lyme in the Netherlands
Transmission of Lyme disease

Lyme disease in Europe is caused by the *Borrelia burgdorferi* sensu lato group; *B. burgdorferi* sensu stricto, *B. afzelii*, *B. garinii*

Transmission by the sheep tick (*Ixodes ricinus*).
Tick Cyclus

Humans are dead-end hosts for *Borrelia burgdorferi* s.l.
Lyme disease

- Early local infection: erythema migrans (EM) 75 - 90% of B. burgdorferi infections
- Early disseminated infection: symptoms of nervous system, skin, joints and heart
- Chronic Lyme borreliosis...
Retrospective GP-study: postal questionnaire

All (± 9,000) general practitioners (GP’s) in 1995, 2002, 2006 & 2010 received pre-coded questionnaire about previous year

Graag verzoek ik u de volgende vragen te beantwoorden:

1. Hoeveel keer bent u in 2005 geconsulteerd voor een tekenbeet?

- [ ] 0 - 1
- [ ] 2 - 4
- [ ] 5 - 14
- [ ] 15 - 24
- [X] 25 - 49
- [X] 50 - 99
- [X] 100 of meer

2. Hoeveel keer bent u in 2005 geconsulteerd voor Erythema Migrans (EM)?

- [ ] 0
- [ ] 1
- [X] 2 - 4
- [ ] 5 - 9
- [X] 10 of meer

3. Hoeveel keer heeft in 2005 uw vermoeden van Lyme geresulteerd in behandeling in het ziekenhuis?

- [ ] 0
- [X] 1
- [ ] 2 - 4
- [ ] 5 - 9
- [ ] 10 of meer

4. Om voornoemde gegevens te interpreteren is het zeer behulpzaam als u uw praktijkomvang wilt aangeven. Hoeveel patiënten staan er ingeschreven in uw praktijk?

- [ ] < 1500
- [ ] 1500 - 1999
- [ ] 2000 - 2499
- [X] 2500 - 2999
- [ ] 3000 of meer
Retrospective GP-study: results

- Population coverage:
  - 88% in 1994
  - 65% in 2009

- Tick bite consultations:
  - 30.000 in 1994
  - 93.000 in 2009

- EM consultations:
  - 6.000 in 1994
  - 22.000 in 2009
Tickbite question in 3 large population studies (>7000)

- Tickbite consultations:
  30,000 in 1994
  ↓
  93,000 in 2009

- Tickbites estimated:
  450,000 in 1994
  ↓
  1,400,000 in 2009

- Tick bite risk on
  EM ~ Lyme: 1994: 1/75 (1.3~1.6%)
  ↓
  2009: 1/65 (1.5~1.8%)
National Tick Bites Study ➔ GP-based prospective study

- 2007 & 2008
  - 700 cases & 500 controls
  - from 300 selected GPs in hotspot areas for tick bites and EM
  - Ticks collected and tested

- Some results
  - 1.8% (9/499) participants with tickbites developed EM
  - 3.7% (3/82) if Borrelia contaminated
  - 0.55% (1/182) if not Borrelia contaminated

In line with GP retrospective study vs 3 large population studies!
- Tick bite risk on Lyme (EM).
  2009: 1/65 (1.5~1.8%)
Intensified Lyme Project, started in 2011

- Work packages
  - Intervention study
  - Mandatory reporting
  - Public Health Impact
  - Communication to the Public
  - Diagnostics
  - Protocol for medical officers
Intensified Lyme Project, started in 2011

● Work packages
  – Intervention study
  – Mandatory reporting
  – Public Health Impact
    ● Retrospective doctors and patient questionnaires
    ● Web-based prospective surveillance
    ● Clinical study
  – Communication to the Public
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  – Protocol for medical officers

After GP-based tick-bites/EM studies

→ Why further study PH impact?
  • Acute manifestations other than EM?
  • Late manifestations?
    ● Higher risk if no EM?
  • Burden of disease?
  • Cost-of-illness?

{ Policy-makers
PH impact: Retrospective doctors and patient questionnaires

incidence & prevalence

burden of disease & cost-of-illness

.............for all Lyme manifestations
Lyme manifestations (acute and late, frequent and rare)

- Erythema migrans (EM)
- Borrelia-lymphocytoma
- Acrodermatitis chronica atrophicans (ACA)
- Neuroborreliosis
- Lyme-artritis
- Lyme-carditis
- Ocular manifestations
- Lyme-encefalopathy
- Persisting Lyme borreliosis
- Persisting complaints after Lyme borreliosis (“post-Lyme” syndrome)
Doctors questionnaires

- ±9000 GPs
- ±1500 Medical officers
- ±5500 Specialists

16,000 total

- Similar questions as in earlier GP-questionnaires
  + number of patients per Lyme manifestation (2009/2010)
  + request to send questionnaires to Lyme patients

→ Should result in:
annual incidence estimates for all Lyme manifestations

and…………..recruitment of patients
Patient questionnaire

- Patients invited by their doctors
  - Lyme complaints in last 12 months
  - 1000-9000 patients....??

→ Should result in:
  - Risk factors for (more severe) manifestations
  - Duration of Lyme manifestations and complaints
  - Burden of disease (Health status)
  - Costs of illness (Health-care consumption, sick leave)
● Also 9000 controls invited
  – normal incidence of (aspecific) complaints
  – not used for burden of disease and cost of illness
Burden of disease

- DALY’s (Disability Adjusted Life Years)

\[
\text{DALY} = \text{YLL} + \text{YLD}
\]

(YLL=Years of Life Lost, YLD=Years Lived with Disability)

**mortality**

\[
\text{YLL} = \sum d_1 \times e_1
\]

d_1 = number of fatal Lyme cases

e_1 = expected life span at age of death

**morbidity**

\[
\text{YLD} = \sum n_1 \times t_1 \times dw_1
\]

n_1 = number of cases with Lyme manifestation

t_1 = duration of Lyme manifestation

dw_1 = disability (severity) weight of manifestation

0=healthy

1=dead (maximum disability)

Disability weights for Lyme.......?
Defining disability weights (0=healthy; 1=dead)

- Valuation of e.g. neuroborreliosis
  - Panel of judges
    - Experts
    - Public
    - Patients
  - Depicting the disease
    - Disease specific
      - e.g. valuating disease specific descriptions by a panel
    - Generic
      - Validated health state questionnaires
  - Valuation method
    - Visual analogue scale (VAS)
    - Time trade off (TTO)
      - for not having a disease/disability, e.g. trade-off 10 years with disease, for 8 healthy years → disability weight = 0.2

Disability weights for diseases are available, e.g.:
- Global Burden of Disease study
- Dutch Disability weights study

But Lyme was not included......
EQ-5D health status questionnaire

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility
- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

Self-Care
- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Usual Activities (e.g. work, study, housework, family or leisure activities)
- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

Pain/Discomfort
- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Anxiety/Depression
- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

- **5 dimensions** (mobility, self-care, usual activities, pain/discomfort, anxiety/depression)

- **3 levels per dimension** (no problems, moderate problems, extreme problems)

\[ 3^5 = 243 \text{ health states} \]

From health state to disability weight?

- **Time-trade-off derived population weight for each element of EQ-5D**

E.g. \( DW_{\text{confined to bed}} = 0.2 \)

(trade-off 10 years confined to bed, for 8 healthy years; and thus give up 2 years of life for avoiding 10 years confined to bed)
Defining Lyme disability weights (0=healthy; 1=dead)

- In summary

1. Lyme patients by manifestation

2. Health state measured \((EQ-5D; 243 \text{ possible health states})\)

3. DW standard for each health state \((Dutch \text{ pop.})\)

4. Disability weights for each Lyme manifestation
Burden of disease

- DALY’s (Disability Adjusted Life Years)

\[
\text{DALY} = \text{YLL} + \text{YLD}
\]

(YLL=Years of Life Lost, YLD=Years Lived with Disability)

- \(\text{YLL} = \sum d_1 \times e_1\)
  - \(d_1\) = number of fatal Lyme cases
  - \(e_1\) = expected life span at age of death

- \(\text{YLD} = \sum n_1 \times t_1 \times \text{dw}_1\)
  - \(n_1\) = number of cases with Lyme manifestation
  - \(t_1\) = duration of Lyme manifestation
  - \(\text{dw}_1\) = disability (severity) weight of manifestation

Disability weights for Lyme manifestations

0 = healthy
1 = dead (maximum disability)
Cost-of-illness (COI)

- Attributing costs to a disease

  - Measure all costs for patients and controls
    - \( \text{COI} = C_{\text{patients}} - C_{\text{controls}} \)
    - E.g. for Alzheimer

  - Measure costs directly related to disease
    - Only patients, no controls
    - Assuming:
      - patients can distinguish Lyme related costs
      - less recall bias than all costs (12 months in retrospective)
Cost-of-illness (COI)

For each Lyme manifestation

› Direct health-care costs
  ● Health care consumption

› Direct non-health-care costs
  ● Transport, housekeeper etc.

› Indirect non-health-care costs
  ● Production loss to society: sick leave

Approach and cost-prices derived from Dutch manual for economical evaluations in health care (www.cvz.nl)
Intensified Lyme Project, started in 2011

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  - Retrospective doctors and patient questionnaires
  - Web-based prospective surveillance
  - Clinical study
→ started last week

- Communication to the Public
- Diagnostics
- Protocol for medical officers

Plans for 2012
PH impact:
Web-based prospective surveillance
Web-based prospective surveillance

- Tick-bite/EM patients recruited by internet
  - “Natuurkalender” tick-bite concept
  + collection of ticks
  + collection EM pictures
  + skin samples EM
  + questionnaires
    › Entering the study
    › 3 months
    › 1 year (or more)

→ This should result in:

- Risk factors for acute and disseminated LB manifestations
  - validation of incidences measured by doctors questionnaire

- Health state over time, medical consumption, sick leave
  - validation of Disease Burden and Cost-of-Illness, no recall bias
PH impact: Clinical study
Clinical study

- In collaboration with Hospitals with a Lyme specialization center
- Inclusion of patients with acute and disseminated LB

→ Should result in:
- Risk factors to develop long-term sequelae
  - Persisting infection/post-Lyme syndrome?

Multi-disciplinary expertises

- Neuropsychology
- Clinical symptoms/treatment
- Microbiology
- Immunology
- Genetics
Intensified Lyme Project, started in 2011

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  - Public Health Impact

In summary **PH impact Lyme study**:

- Incidence of Lyme manifestations other than EM
- Risk factors for more severe disease
- Burden of Disease
- Cost-of-illness

Conclusions and results

Next year and the years to come........
Acknowledgments

National Institute of Public Health (RIVM)
- Florianne Bauer
- Agnetha Hofhuis
- Wilfrid van Pelt

- Ardine de Wit (burden of disease/cost-of-illness)
- Mirjam Kretzschmar (burden of disease/cost-of-illness)
- Arie Havelaar (burden of disease/cost-of-illness)

NVLP
- Diana Uitdenbogerd (Lyme patient federation)

Erasmus MC, Rotterdam
- Juanita Haagsma (burden of disease/cost-of-illness)

Stigas
- Ad de Rooij (medical officers point of view)

Kees.van.den.wijngaard@rivm.nl